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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,432	10/27/2005	Svend Kaasgaard	10300.204-US	7515
25908 7590 05/10/2010 NOVOZYMES NORTH AMERICA, INC. 500 FIFTH AVENUE SUITE 1600 NEW YORK, NY 10110				
EXAMINER				
GOUGH, TIFFANY MAUREEN				
ART UNIT		PAPER NUMBER		
1657				
NOTIFICATION DATE		DELIVERY MODE		
05/10/2010		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents-US-NY@novozymes.com

### Office Action Summary

**Application No.**

10/519,432

**Applicant(s)**

KAASGAARD ET AL.

**Examiner**

TIFFANY M. GOUGH

**Art Unit**

1657

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 28 January 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 14-30 and 32-36 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 14-30 and 32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

Applicant's response filed 1/28/2010 has been received and entered into the case. Claims 14-30, 32-36 are pending and have been considered on the merits. All arguments and amendments have been considered.

***New rejections necessitated by amendment***

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 36 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 36 recites "...wherein the compound is low metabolizable measured by (OD3-OD2)/(OD1-OD2) less than 25%...". Given the compounds disclosed within applicants Markush group of claim 36, and the recitation of "wherein the compound is low metabolizable measured by ...", it would appear as if the compounds listed would inherently possess the OD value as claimed by applicant.

Also "low metabolizable...<25%" is unclear because it does not indicate whether applicant is claiming a specific number less than 25, or if "low metabolizable" is specifically defined by the term "<25%" as a whole.

The term "low" in claim 36 is a relative term which renders the claim indefinite. The term "low" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 36 is rejected under 35 U.S.C. 102(b) as being anticipated by Tothill et al. (Enzyme and Microbial Technology, 1997, p. 590-596).

Applicant claims a fermentation method comprising adding to a culture medium of at least 50 liters one or more compounds in the amount of at least 0.1%(w/w) selected from 1,2-propandiol, 1,3-propandiol, ethylene glycol, trehalose, xylitol, arabitol, dulcitol, mannitol, erythritol, cellobiose, sorbitol and a polyether having an average molecular weight less than 1000, either before and/or during fermentation.

Tothill teach a fermentation method of bacteria and yeasts comprising adding polypropylene glycol and a salt before and/or during fermentation to the 60 liters of fermentation medium (see p. 591-592, Materials and Methods section).

Thus, the reference anticipates the claimed subject matter.

Claim 36 is rejected under 35 U.S.C. 102(b) as being anticipated by Clarke et al. (US 5260202).

Clarke teach adding to a fermentation broth before fermentation, polypropylene glycols in addition to a salt (col. 4, example 1, col. 5, 6).

Thus, the reference anticipates the claimed subject matter.

Claim 36 is rejected under 35 U.S.C. 102(b) as being anticipated by DD 0153495.

DD '495 teaches a fermentation method comprising adding polypropylene glycol before and/or during fermentation to at least 50 liters of fermentation medium (see Example 2).

Thus, the reference anticipates the claimed subject matter.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14-30, 32-36 are rejected under 35 U.S.C. 103(a) as being obvious over Kaasgaard et al. (US2004/0175812A1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing

that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

Applicant claims a method for fermenting a bacterium, specifically *Bacillus* sp., producing an enzyme of interest, specifically a hydrolase, in a culture medium of at least 50 liters comprising adding one or more compounds in the amount of at least 0.1%(w/w) selected from 1,2-propandiol, 1,3-propandiol, ethylene glycol, trehalose, xylitol, arabitol, dulcitol, mannitol, erythritol, cellobiose, sorbitol and a polyether having an average molecular weight less than 1000, either before and/or during fermentation. Applicant also claims addition of a salt to the medium, such as a chloride, sulphate, phosphate, nitrate, and ammonium salt. The enzyme of interest, a hydrolase, is recovered after removal of the bacterium.

Kaasgaard et al teach a method of recovering a protein of interest by the addition of compounds, specifically polyols and carbohydrates including, trehalose, xylitol, erythritol, sorbitol, monopropylene glycol, i.e. 1,2-propanediol to a bacterial fermentation medium during fermentation wherein an enzyme of interest is recovered (see abstract, 0007-0009, 0051-0057, 0080-0096, claims 1-18) after the removal of the bacterium. They disclose the bacteria to be of the *Bacillus* genus and the enzyme to be a hydrolase (see 0007-0022). They also teach the addition of salts such as chloride, sulphate, phosphate, nitrate, and ammonium salt (see 0106-0108). The polyol is added in an amount of at least 0.1%(w/w) of medium (see 0093).

Kaasgaard et al do not teach each and every compound, specifically, 1,2 and 1,3-propanediol, arabitol, dulcitol and polyethers with a MW less than 1000. However,

they do teach any polyol having the formula  $C_nH_{2n+2}O_n$  and/or a carbohydrate.

Thus, the compounds claimed fall within this formula, thus, all the claimed polyols and carbohydrates would be obvious to one of ordinary skill in the art to be added to a fermentation solution to recover an enzyme of interest. Further, as stated in the previous Office actions, propylene glycols, such as 1,2 propandiol are known in the art to be the collective name for monopropylene glycols, thus, 1,2 and 1,3 propandiols would inherently be covered by the term monopropylene glycol.

### ***Response to Arguments***

**Applicant's arguments and Declaration filed 1/28/2010 have been fully considered but they are not persuasive.** Applicant argues that '812 does not teach or fairly suggest adding a polyol to a culture medium before and/or during fermentation in a process of fermenting a bacterium specifically for producing an enzyme of interest and that the benefits of doing so would not be predictable.

Applicants arguments are not persuasive because as stated above, it is noted that '812 teaches recovering a protein of interest from a fermentation broth (0044), they do however teach adding a polyol to a culture solution **prior to the recovery step**, i.e. during fermentation (0007,0009,0070). Clearly, if the art is teaching recovering a protein of interest from a fermentation broth prior to the recovery step, the addition of polyols before the recovery step can only be occurring during fermentation. **Further, there is nothing in the disclosure of '812 which precludes fermentation from continuing, i.e. nothing in method teaches stopping fermentation. '812 clearly**



**teaches adding prior to the recovery process.** Applicant states in the arguments, p.6 first paragraph, that "One of ordinary skill in the art of making enzymes would understand that fermentation occurs before the recovery of enzyme." Thus, one of skill in the art would be motivated to add a polyol to a fermentation broth because polyols are known in the art to be useful in increasing solubility of a protein of interest (0007) and keeping the protein in solution to prevent crystallization of protein during the fermentation process. It does not appear that adding a polyol during any point of the fermentation process would effect its respective function.

Claims 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over CH667673.

CH 667673 teaches adding to a 40 ml fermentation broth before fermentation, polypropylene glycols in addition to an ammonium or nitrate salt (see translated p. 4-6).

CH673 does not teach at least 50 liters, however, it is well within the purview of one of skill in the art to practice the invention of '673 on a large scale. Clearly one of skill is aware of scaling up fermentation broths. Further, it is well known that hydrolases are commonly produced during fermentation, note that hydrolase is merely claimed as an enzyme of interest.

A holding of obviousness is therefore required.

Claims 14, 15, 17, 18, 19, 20, 24, 29, 30, 34, 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clarke et al. (US 5260202).

Clarke teach adding to a fermentation broth before fermentation, polypropylene glycols, sugars, polyols, ethylene glycol and sorbitol in addition to a salt (col. 2, lines 7-20, col. 4, example 1, col. 5, 6).

Clarke does not teach at least 50 liters, however, it is well within the purview of one of skill in the art to practice the invention of Clarke on a large scale. Clearly one of skill is aware of scaling up fermentation broths.

A holding of obviousness is therefore required.

Claims 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of DD 0153495 in view of each of Schreiber (U.S. Patent 4,016,039), Brothers et al (U.S. Patent 4,673,647), GB 1001173 in further view of Boyer et al (U.S. Patent 5,385,837).

Applicant claims a method for fermenting a bacterium, specifically *Bacillus* sp., producing an enzyme of interest, specifically a hydrolase, in a culture medium of at least 50 liters comprising adding one or more compounds in the amount of at least 0.1%(w/w) selected from 1,2-propandiol, 1,3-propandiol, ethylene glycol, trehalose, xylitol, arabitol, dulcitol, erythritol, sorbitol and a polyether having an average molecular weight less than 1000, either before and/or during fermentation. Applicant also claims addition of a salt to the medium, such as a chloride, sulphate, phosphate, nitrate, and ammonium salt. The enzyme of interest, a hydrolase, is recovered after removal of the bacterium.

DD '495 teaches a fermentation method comprising adding polypropylene glycol before and/or during fermentation to at least 50 liters of fermentation medium (see Example 2).

DD' 495 does not teach adding the additional components to the fermentation medium.

Schreiber disclose a process for the recovery of proteins, specifically proteases, from fermentation solutions containing polyoxyethylene glycol, i.e. polyethylene glycol, having a low molecular weight between 500-800 in the amount of up to 3% by weight and salts such as sulphate and chloride salts(see abstract and column 1, lines 10-13). Schreiber teaches adding the polyol to the fermenter solution before precipitation and filtration. They teach that the improvement is found in adding the polyol to the fermentation solution **before** adding an inorganic salt (see claim 1 and example 1), and **before** precipitation (see abstract).

Brothers et al disclose a process for the recovery of enzymes obtained from a fermentation medium from a microorganism of interest. Brothers differs from the claims in that, although they disclose any polyol and more specifically low molecular weight polyethylene glycol, 1-2,propandiol, and the C2 through C8 alcohols having at least two OH groups may also be used. Such polyols include propylene glycol, glycerol, the low molecular weight (900 or less) polyethylene glycols and mixtures thereof, therefore, sugar alcohols such as xylitol, arabitol, dulcitol, erythritol, and sorbitol, may be used during the enzyme preparation. They do not specifically state trehalose, xylitol, arabitol, dulcitol, erythritol, and sorbitol, however, xylitol, arabitol, dulcitol, erythritol, sorbitol and

polyethers having an average molecular weight of less than 1000 meet the disclosed characteristics and would therefore be obvious to use such sugar alcohols. They teach adding a polyol solution, preferably low molecular weight polyethylene glycol, 1-2,propandiol, and the C2 through C8 alcohols having at least two OH groups. Such polyols include propylene glycol, glycerol, the low molecular weight (900 or less) polyethylene glycols and mixtures thereof (see column 5, lines 3-53) after fermentation to obtain the enzyme of interest. However, they teach these compounds to be important in obtaining an enzyme of interest in a fermented solution.

It would be obvious to one of ordinary skill in the art to add these compounds to a fermented composition to obtain a protein, i.e. enzyme during fermentation rather than "after" because these compounds are known in the art to be useful in recovering enzymes in a solution, i.e. solubilizing an enzyme of interest (col 4, lines 53-62). Further, DD '495 teaches an improvement in fermentation methods by adding polypropylene glycol to a fermentation medium.

Thus, one of ordinary skill in the art at the time of the invention would have been motivated to use polyols disclosed in the art with a reasonable expectation of success in obtaining an enzyme of interest from a fermentation solution.

Further support of the use of carbohydrates and salts in a fermentation medium to obtain an enzyme of choice from a microorganism is disclosed by Boyer et al. They disclose obtaining an alkaline protease from *Bacillus proteolyticus* culture containing substrates such as trehalose (see Table 1) and salts such as potassium phosphate,

calcium chloride, sodium sulphate and magnesium sulphate (see abstract and column 5, lines 65 continued to column 6, up to lines 56).

It is well established that duplicating compounds or components with similar functions within a composition is obvious; see *In re Harza*, 274F.2d 669,124 USPQ 378 (CCPA 1960) and MPEP 2144.04. **Polyols, i.e. sugar alcohols were known in the art at the time of the invention to solubilize and recover enzymes (see Brothers et al. column 5, lines 20-27, Schreiber, abstract and col. 1, lines 10-13, GB1001173, and Boyer et al).**

It is well known that it is *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. *In re Pinten*, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); *In re Susi*, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); *In re Crockett*, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960).

One of ordinary skill in the art would therefore have been motivated by the combined disclosures of the references of the addition of many carbohydrates i.e. polyols and sugar alcohols to fermentation mediums during and after fermentation to obtain an enzyme of interest, more specifically the addition of claimed polyols, which are disclosed as being acceptable and successful in obtaining enzymes from fermentation solutions.

Therefore, the claimed invention as a whole is prima facie obvious over the prior art.

### ***Response to Arguments***

Applicant's response filed 1/28/2010 does not provide any arguments regarding the above rejections. Applicants merely urge reconsideration. Reconsiderations have been given to the previously presented and newly added claims. The rejections of record are necessitated by applicants claim amendments.

### ***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIFFANY M. GOUGH whose telephone number is (571)272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Weber Jon can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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